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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,789	08/19/2002	Toshio Miyata	SHIM1130	1099

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 08/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,789	MIYATA, TOSHIO	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,12 and 15-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/22/05; 11/3/04;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FD

DETAILED ACTION

The allowance of claims 7, 9, 12, and 15-38 has been withdrawn in light of new relevant prior art and examination has been reopened. The Request for Continued Examination (RCE) filed on April 22, 2005 is therefore inappropriate.

Clams 1-6, 8, 10, 11, 13-14 have been cancelled by the Applicant. Claims 7, 9, 12, 15-38 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 7, 9, 12, 15-17, 19-24, and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyata, T. et al. (*Kidney International*, **1999**, *55*, pp 389-399) in view of Ruggiero-López, D. et al. (*Biochem. Pharmacol.* **1999**, *58*, pp 1765-1773).

Applicant's claim reads on a carrier immobilized with one or more biguanide agents wherein the shape of the carrier is selected from the group: membranous,

fibrous, granular-shaped, hollow fiber-like, non-woven fabric-like, porous, and honeycomb-shaped.

Miyata et al. teach that Advance Glycation End products (AGEs) are linked to plasma proteins (mainly albumin). These AGEs are not effectively removed by hemodialysis and peritoneal dialysis and accumulate in blood and peritoneal dialysate. AGE accumulation in plasma proteins cannot by attributed to decreased renal clearance of protein-linked carboxymethyllysine (CML) and pentosidine (last sentence of the 3rd paragraph in the right hand column on page 390). AGEs have been implicated in the pathogenesis of several diseases, including diabetes and uremia (1st sentence in the body of the text on page 389, left hand column). The formation of AGEs is associated with the increased concentration in blood plasma of small reactive carbonyl compounds (4th sentence in left hand column on page 389).

Miyata, T. et al. suggest the development of less toxic more specific carbonyl stress inhibitors immobilized in cartridges may enhance extraction of reactive carbonyl compounds from blood during dialysis for the treatment of conditions in which reactive carbonyl compounds and carbonyl stress end products are implicated such as diabetes, atherosclerosis, neurodegenerative diseases, and even chronic age-dependent chemical modifications of tissue proteins (Last three sentences in the subsection entitled, "Carbonyl stress quenching" on page 396). The term cartridge is interpreted to read on a carrier having one of the shapes listed in claim 7. The phrase "enhance extraction of reactive carbonyl compounds from blood during dialysis" implies the use of a hemodialysis membrane.

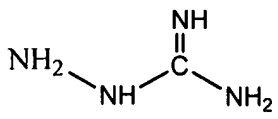
Miyata, T. teaches that carbonyl stress end products are formed by carbonyl amine chemistry between carbonyl compounds and protein amino groups (1st sentence of the section entitled, "Carbonyl stress quenching" on page 396). Ketones and aldehydes are examples of carbonyl compounds that have a well known reaction chemistry with primary amino groups to yield imines, also called Schiff bases, whereas their reaction with hydrazine and its derivatives results in compounds called hydrazones (Solomon, T. W. G *Organic Chemistry, 5th edn.* John Wiley & Sons, Inc.: New York, 1992, pp 701-704).

Miyata, T. teaches that aminoguanidine and thiazolidine derivatives (e.g. OPB-9195, also called, ±2-iso-propylidenehydrazono-4-oxo-thiazolidin-5-ylacetanilide) have been used to inhibit carbonyl stress by a similar mechanism, read as the reaction of their hydrazine nitrogens with reactive carbonyl species to form hydrazones (sentences 2-5 in the section entitled, "Carbonyl stress quenching" on page 396).

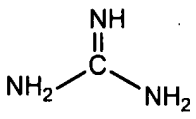
Miyata lacks in the specific teaching or suggestion of using a biguanide compound to inhibit carbonyl stress. Miyata also does not state the shape of the cartridge he suggests should contain immobilized carbonyl removing agents.

Ruggiero-Lopez, D. et al. teach the chemical structures of aminoguanidine and metformin (dimethylbiguanide) and that these compounds are guanidine derivatives (Fig. 1, pg 1766, right hand column; see the structures below).

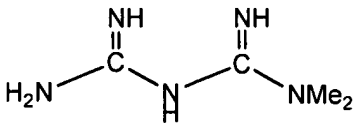
Aminoguanidine



Guanidine



Metformin (a biguanide)



Ruggiero-Lopez teaches that metformin was first introduced into clinical practice in 1957 as an oral hyperglycemic agent for the management of non-insulin dependent diabetes mellitus (page 1766, 5th sentence in the second paragraph in the left hand column of said page).

Ruggiero-Lopez teaches that aminoguanidine is the most studied guanidine compound with a clear inhibitory effect on AGE formation and that several groups have shown that it was quite effective in inhibiting the formation of AGEs *in vitro* and *in vivo* (3rd and 4th sentences in the Discussion section, located in the right hand column on page 1769).

Ruggiero-Lopez teaches that the presence of the guanidine group in the metformin structure confers a potential use of this drug for the inhibition of the Maillard reaction via reaction with carbonyl groups of reducing sugars and dicarbonyl compounds and that biguanides have been shown to react with α-diketones in strongly alkaline ethanolic media (6th and 7th sentences in the Discussion section located in the left hand column on page 1769).

Ruggiero-Lopez teaches that substantial recent data indicate the mediation of glucose toxicity through the increased production of highly chemically reactive α-dicarbonyl precursors of AGE (Advanced Glycation End products) (1st sentence of the second paragraph on the bottom right hand side of page 1765).

Ruggiero-Lopez teaches that glyoxal is more reactive with proteins than glucose and seems to be a major α-dicarbonyl formed in glucose auto-oxidation, a process which could contribute to sugar protein modification in diabetes (1st paragraph beginning

on the bottom right hand column on page 1765 which continues onto the top left hand column of page 1766).

Ruggiero-Lopez teaches that methylglyoxal is another reactive carbonyl compound whose level is increased in diabetes, which can react with amino groups of proteins generating AGEs (1st paragraph beginning at the top of the left hand column on page 1766). He also states that recent reports show evidence of methylglyoxal-derived modification in human tissues and that this supports the occurrence of *in vivo* dicarbonyl-mediated protein reaction by the Maillard reaction (Last sentence of the 1st paragraph beginning on the left hand column of page 1766).

Ruggiero-Lopez teaches that the results of their experiments suggest metformin inhibits the glycoxidation of albumin by glyoxal and methylglyoxal via reaction of its guanidino moieties with the carbonyl groups of methylglyoxal and glyoxal (1st sentence of the 1st paragraph beginning on page 1772, in the left hand column).

Ruggiero-Lopez teaches others have reported on metformin's inhibitory effect on the glycoxidation of albumin by glucose under aerobic conditions where glyoxal is formed (4th sentence of the 1st paragraph beginning on page 1772, in the left hand column).

Ruggiero-Lopez teaches that recent results from the UKPDS (UK Progressive Diabetes Study) trial have shown that metformin significantly reduced the mortality risk of NIDDM (Non-Insulin Dependent Diabetes Mellitus) patients, suggesting it has additional effects, besides its known antihyperglycemic effects (e.g. as a carbonyl stress inhibitor) (1st sentence beginning on page 1773 in the left hand column).

Ruggiero-Lopez teaches that their results are relevant for a potential clinical use of metformin in the prevention of diabetic complications by inhibition of carbonyl stress (last sentence in the last paragraph on page 1773).

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Miyata and Ruggiero-Lopez to alleviate the carbonyl stress state in a person's blood via hemodialysis or contacting their blood or peritoneal dialysate with a carrier comprised of immobilized AGE-inhibitors, such as the biguanide, metformin. The motivation to combine these teachings comes from Miyata who teaches the need to inhibit the formation of AGEs and promote their removal from blood and peritoneal dialysate. Miyata also states that hemodialysis and peritoneal dialysis are unable to remove AGEs and suggests that this problem could be addressed by immobilizing carbonyl stress inhibitors in cartridges used during dialysis therapy. Motivation for an ordinary artisan in the art to use biguanide agents immobilized in a carrier to remove AGEs *in vivo* is provided by Ruggiero-Lopez who teaches that metformin was able to inhibit the formation of albumin-AGEs and suggested its potential clinical use in the prevention of diabetic complications by inhibition of carbonyl stress. Miyata and Ruggiero-Lopez are lacking in the teaching of a specific carrier shape and the motivation to modify the carrier's physical shape and dimensions. An ordinary person of skill in that art at the time of the instant invention would have had a reasonable expectation of success in using carriers containing immobilized biguanide agents to remove AGEs, because Ruggiero-Lopez' results suggest that both aminoguanidine and metformin consume reactive carbonyl

compounds that lead to the formation of AGEs and aminoguanidine is a well known carbonyl stress inhibitor. The skilled artisan would also have been motivated to administer metformin orally to inhibit carbonyl stress, because it has been used as an oral antihyperglycemic agent in clinical practice since 1957 and has recently been shown to have anti-glycative effects (i.e. it consumes reactive carbonyls and inhibits the formation of AGEs).

Secondly, the choice of carrier shape and any subsequent modification of a carrier's shape and physical dimensions, such as length, diameter, and thickness are considered obvious routine modifications to optimize the performance of materials used in various processes. For example, if one had a square-shaped carrier and needed a spherical-shaped carrier for use in a different dialysis machine, one would appropriately adjust the carrier shape and dimensions to conform to the physical constraints of the carrier location within the different dialysis machine (e.g. shape, size, length, thickness, etc.). Increasing or decreasing the size of a given material used would also change its surface area. Therefore, changing surface area is also an obvious routine modification in the art.

Claims 18 and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyata, T. et al. (*Kidney International*, **1999**, *55*, pp 389-399) and Ruggiero-López, D. et al. (*Biochem. Pharmacol.* **1999**, *58*, pp 1765-1773) and in view of Keogh (U.S. patent 5,928,916).

Applicant's claims read on carriers of various shapes (membranous, fibrous, honeycomb, hollow fiber-like, non-woven fabric like) and materials (inorganic &

synthetic/natural polymers) on which one or more biguanides (e.g. metformin) have been immobilized by a variety of means (e.g. physical adsorption, biochemical binding reaction, ion binding, covalent binding, or grafting).

The teachings of Miyata, T. in view of Ruggiero-Lopez have been set forth above. Several salient features of their teachings are highlighted below.

Miyata, T. suggests the development of less toxic more specific carbonyl stress inhibitors **immobilized in cartridges** may enhance extraction of reactive carbonyl compounds from blood during dialysis for the treatment of conditions in which reactive carbonyl compounds and carbonyl stress end products are implicated such as diabetes, etc. (Last three sentences in the subsection entitled, "Carbonyl stress quenching" on page 396). The term cartridge is interpreted to read on a carrier having one of the shapes listed in claim 7. The phrase "enhance extraction of reactive carbonyl compounds from blood during dialysis" implies the use of a hemodialysis membrane.

Ruggiero-Lopez teaches that the biguanide metformin is a **guanidine derivative** (Fig. 1, pg 1766, right hand column; see structures on pg 4 of this action).

Ruggiero-Lopez teaches that their results are relevant for a potential clinical use of metformin in the prevention of diabetic complications by inhibition of carbonyl stress (last sentence in the last paragraph on page 1773).

The combined teachings of Miyata and Ruggiero-Lopez are lacking in the means of immobilizing biguanide agents onto carriers of various shapes and materials.

Keogh (U.S. patent 5,928,916) teaches a method involving combining at least one biomolecule comprising a negatively charged moiety with a material comprising at

least one positively charged **biguanide moiety** ($RNHC(NH)NHC(NH)NH_2$) to form an immobilized biomolecule on a medical device biomaterial surface through an ionic bond (column 3, lines 15-22; claims 1a and 2).

Keogh teaches that a "biomaterial" is a material that is substantially insoluble in body fluids and that is designed and constructed to be placed in or onto the body or to contact fluid of the body (column 3, lines 59-62),

Keogh teaches that the guanidinium group's features make it a very attractive moiety for incorporation onto biomaterial surfaces. For example, its high basicity (a pK_a of 13.5 for guanidinium itself) allows it to remain protonated over a much wider range of pH than does the ammonium group. In fact, at physiological pH, all but a small fraction of the guanidine molecules will exist as positively charged species (column 4, lines 51-57). Metformin contains two guanidine-derived groups.

Keogh teaches biomaterials that comprise amines on their surface may be modified to comprise guanidino moieties by reaction with O-methylisourea or S-methylisothiourea to yield substituted guanidines (column 5, lines 6-8). This modification would be a means to covalently attach a biguanide to a biomaterial surface comprising amines.

Keogh teaches that biomaterials of the present invention not containing amines on their surface may be aminated readily through a number of methods well known in the art (column 5, lines 41-43). This teaching increases the number of biomaterials that could be used as carriers upon which biguanides could be immobilized.

Keogh teaches that there are a number of methods well known in the art to functionalize various moieties to monoguanidines or **biguanides (diguanides)** (column 5, lines 63-67 and column 6, lines 1-9).

Keogh teaches that molecules containing at least one guanidino moiety and at least one reactive moiety may be **grafted** to a biomaterial surface through the reactive moiety (column 6, lines 10-12). Metformin and other biguanides contain at least one guanidino moiety.

Keogh teaches that compounds such as 1-dodecylguanidine which comprise at least one guanidino moiety and a hydrophobic region may be adsorbed from a solution onto the surface of a hydrophobic biomaterial (column 6, lines 38-41). Biguanides contain at least one guanidino moiety and can be appropriately derivatized to contain a hydrophobic region. Adsorption reads on the term "physical adsorption."

Keogh teaches that biomaterials may be furnished with a net negative charge on their surface, such as polyethylene following exposure to sulfuric acid comprising potassium permanganate, and may be exposed subsequently to guanidino comprising compounds, thereby reversing the surface polarity of the biomaterial surface from negative to positive (column 6, lines 52-57).

Keogh teaches that his method can be used to modify several different substrates, for example, metals, such as titanium, titanium alloys, TiNi alloys, shape memory alloys; **aluminum oxide (i.e. alumina)**, pyrolytic carbon, glassy carbon; **polymers,** such as polyamides, polycarbonates, polyethers, polyesters, polyolefins, rubber; **minerals** or **ceramics,** such as hydroxapatite; human or animal protein or

tissue, such as bone, skin, teeth, collagen, laminin, elastin or fibrin; **organic materials,** such as wood, **cellulose** or compressed carbon; and other materials such as **glass** (column 8, lines 11-28). Alumina, metals, hydroxyapatite, ceramics, and glass are examples of inorganic materials. Polyamides, polycarbonates, etc. are examples of synthetic organic macromolecules. The term "macromolecule" is synonymous with the word "polymer." Cellulose is an example of a naturally occurring polysaccharide.

A person of ordinary skill in the art at the time of the instant invention would have been motivated to combine the teachings of Miyata, Ruggiero-Lopez, and Keogh because all these inventors teach the use of guanidine-containing compounds for use in medical applications. Miyata provides the motivation for the immobilization of carbonyl stress inhibitors in carriers such as cartridges (supra) and Ruggiero-Lopez provides the motivation for using biguanides to this effect in dialysis therapy in which body fluids (e.g. blood, blood plasma, peritoneal dialysate) would contact carbonyl stress inhibitors. Keogh's teachings would have allowed an artisan of ordinary skill in the art to immobilize biguanides on to biomaterials, use these modified materials as carriers to contact body fluids, remove reactive carbonyl compounds from said fluids and have a reasonable expectation of success. The immobilized biguanide agents are expected to remain positively charged and thus immobilized on the carriers used when exposed to body fluids at physiological pH conditions.

Claims 34-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ikeda, H. et al. (U.S. patent 5,952,356) in view of Ruggiero-López, D. et al. (*Biochem. Pharmacol.* **1999**, *58*, pp 1765-1773).

Applicant's claim reads on a method of removing carbonyl compounds comprising contacting one or more biguanide agents with or more body fluid (blood, blood plasma, or peritoneal dialysate) via the administration of the biguanide agent by injection.

Applicant's claim does not require immobilization of the biguanide, nor does it specify any carrier for administration of the biguanide agent. The intended use of the biguanide agent for the removal of carbonyl compounds is not given any weight in the evaluation of the claim, as this is considered a property of these compounds. Therefore, the key component of the method of claim 38 comprises contacting one or more biguanide agent with one or more body fluid via an injection.

Ikeda, H. et al. teach a pharmaceutical composition which comprises an insulin sensitivity enhancer in combination with at least one member of the group consisting of an α-glucosidase inhibitor, an aldose reductase inhibitor, a **biguanide**, a statin compound, a squalene synthesis inhibitor, a fibrate compound, a LDL catabolism enhancer and an angiotensin converting enzyme inhibitor (column 2, lines 1-8).

Ikeda teaches that **biguanides** are drugs having actions of stimulation of anaerobic glycolysis, increase of the sensitivity to insulin in the peripheral tissues, inhibition of glucose absorption from the intestine, suppression of hepatic gluconeogenesis, and inhibition of fatty acid oxidation (column 11, lines 46-50).

Ikeda teaches that some examples of biguanides are **phenformin, metformin, and buformin** (column 11, lines 50-51).

Ikeda teaches that the dosage form for said pharmaceutical composition includes such oral dosage forms as granules, powders, tablets, capsules, syrups, emulsions, suspensions, etc. and such non-oral dosage forms as **injections (e.g. subcutaneous, intravenous, intramuscular and intraperitoneal injections)**, drip infusions, external application forms (e.g. nasal spray preparations, transdermal preparations, ointments, etc.), and suppositories (e.g. rectal and vaginal suppositories). These dosage forms can be manufactured by the per se known technique conventionally used in pharmaceutical procedures (column 13, lines 51-58).

Ikeda teaches that his pharmaceutical compositions have a low toxicity and can be used safely in mammals (e.g. humans, etc.) (column 14, lines 58-60).

Ikeda lacks in the express teaching that biguanide agents also function as carbonyl stress inhibitors.

Ruggiero-Lopez teaches that their results are relevant for a potential clinical use of **metformin** in the prevention of diabetic complications by **inhibition of carbonyl stress** (last sentence in the last paragraph on page 1773). Metformin is a biguanide agent.

A person of ordinary skill in the art at the time of the instant invention would have been motivated to use Ikeda's invention in view of the teachings of Ruggiero-Lopez to administer a biguanide agent via an injection in order to capitalize on the known carbonyl stress inhibition properties of metformin and other biguanides (as set forth above on page 9 of this action). It is understood that a non-oral dosage formulated for injections, such as an intravenous injection of Ikeda's invention, would result in the

contact of one or more biguanides with a body fluid, such as blood, blood plasma, and peritoneal dialysate. An artisan in the art at the time of the instant invention would therefore have had a reasonable expectation of success of contacting one or more body fluids via the administration by injection of one or more biguanide agents to affect the inhibition of carbonyl stress.

Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the art.

Art of Interest

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The following references are considered relevant to the evaluation of the instant application: http://www.fmc-ag.com/internet/fmc/fmcag/agintpub.nsf/Content/Modern_hemodialysis_+the_first_hollow-fiber_dialyzers_2004 ; http://www.fmc-ag.com/internet/fmc/fmcag/agintpub.nsf/Content/The_first_successful_dialysis_treatment%3A_Willem_Kolff_2004 ; Lemke et al. (U.S. patent application 2003/0171502 A1), and Tanaka, Y. et al. (*Current Therapeutic Research: Clinical and Experimental*, **1997**, *58(10)*, 693-697.) The first two references are relevant because they provide useful information as to the history of the state of the art of hemodialysis in various decades. Lemke et al. is relevant because it discusses the removal of AGE precursors from blood, plasma, and PBS buffer by reaction of diaminoguanidine and/or triaminoguanidine. Biguanides are considered guanidine derivatives. The last is of

interest, because it reports on the inhibitory effects of metformin on the formation of advanced Glycation end products.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

This is a provisional obviousness-type double patenting rejection, because the conflicting claims have not been patented.

Claims 32-38 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13, 14, 20-23, 28-31, 36-38, and 45 of copending Application No. 11,093,950. Although the conflicting claims are not identical, they are not patentably distinct from each other because they have similar and mutually overlapping scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Independent claims 32 and 34 of the instant application are drawn to methods of removing carbonyl compounds comprising contacting a carrier, upon which a biguanide agent has been immobilized, with one or more body fluids selected from blood, blood plasma, and peritoneal dialysate. The term "carrier" encompasses both soluble and insoluble carriers. The term carrier encompasses an adsorbent cartridge. Biguanides are carbonyl-trapping agents, and therefore these compounds remove carbonyl compounds. Contacting a carrier containing immobilized biguanide agents, which are carbonyl trapping-compounds, with a body fluid, such as peritoneal dialysate, would yield peritoneal dialysate with a reduced carbonyl content.

Independent claims 13, 21, 29, and 38 of '950 are drawn to methods of preparing peritoneal dialysates having reduced carbonyl content comprising (a) contacting the peritoneal dialysate with the surface of an insoluble carrier having immobilized thereon a carbonyl compound-trapping agent and (b) separating the peritoneal dialysate from the surface having the carbonyl compound.

The independent claims of both the instant application and '950 are drawn to methods of removing carbonyl compounds from peritoneal dialysate via contacting said dialysate with a surface having the ability to remove carbonyl compounds due to the presence of carbonyl compound-trapping agents. The critically important criteria of both claim sets are (1) contacting the peritoneal dialysate with said surface and (2) the removal of carbonyl compounds from the dialysate. Both claim sets satisfy these critically important criteria. Although the two claim sets are not identical, the independent claims of the instant application and '950 have similar, and therefore,

overlapping scope. The relevant dependent claims of both applications are considered to have overlapping steps, components, and scope as well.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JHAA

Gary d. Kunz

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TECHNOLOGY CENTER 1600